

EXHIBIT 29

Migration of a Particulate Radioactive Tracer from the Vagina to the Peritoneal Cavity and Ovaries

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SUMMARY

In this report we describe a radionuclide procedure designed to evaluate the migration of a particulate radioactive tracer from the vagina to the peritoneal cavity and ovaries, as well as the determination of the patency of the pathways between these two extremes of the female reproductive system.

99m Tc-labelled human albumin microspheres (99m Tc-HAM) were deposited in the posterior fornices of 24 patients a day before they were to undergo different gynaecological operations. During this period sequential images were obtained and after the operation radioactivity levels in the removed organs and tissues were counted with a scintillation detector.

In 14 out of 21 cases, the ovaries and fallopian tubes were counted separately from the uterus. Nine were positive (radioactivity levels were sufficiently high in the tubes and ovaries) and 5 were negative (no substantial radioactivity levels could be detected in either the tubes or the ovaries). The 5 negative results all occurred in patients with proved tubal damage as a result of previous infection.

All the results were either true positive or true negative, providing evidence of migration, or obstruction, of 99m Tc-HAM from the vagina through the uterus and tubes to the peritoneal cavity and ovaries.

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In the female, the peritoneal cavity is linked with the outside via the fallopian tubes, the uterus and the vagina, and there is evidence of migration of different substances in either direction. For example, malignant cells from ovarian carcinoma can be demonstrated in the posterior fornix of the vagina.¹ After menstruation the gonococcus can penetrate the cervix and gain access through the uterus and tubes to the peritoneal cavity and ovaries.² For pregnancy to occur, spermatozoa have to move up the uterus and the ova down the tube. Retrograde menstruation is also a well-known phenomenon. After insufflation, air and gases pass easily from the vagina into the peritoneal cavity up to the diaphragm. Radio-opaque contrast media are introduced with great ease through the uterus and

tubes into the peritoneal cavity, and tubal patency is easily demonstrated during peritoneoscopy by injection of a dye through the cervix and into the tubes.³

Does this also hold for inert chemical substances? Will a chemical substance deposited in the vagina later appear in the peritoneal cavity? Such migration could well explain the aetiological role of chemical substances in certain gynaecological diseases. It has already been suggested that talcum powder is one of these potentially dangerous inert chemical products. Electron micrographic slides of removed human ovaries have shown asbestos particles resting on them, and there is evidence that these particles originated from talc used to dust condoms.⁴

To demonstrate the upward migration of chemical substances we made use of radionuclide imaging and counting techniques.

MATERIAL AND METHODS

The subjects of this study were 24 adult women, both Blacks and Whites, from the Academic Hospitals of the University of the Orange Free State in Bloemfontein. All had been admitted to hospital for elective gynaecological surgical operations (Table I). The radionuclide procedure was explained and the necessary consent obtained.

TABLE I. SURGICAL INDICATION AND OPERATIVE PROCEDURE

Number of patients	Surgical indication	Operative procedure
4	Sterilization	Fimbriectomy
7	Ca. breast stage III	Bilateral salpingo-oophorectomy
1	Ca. breast stage III	Hysterectomy and bilateral salpingo-oophorectomy
2	Postmenopausal bleeding	Dilatation and curettage
2	Postmenopausal bleeding	Hysterectomy and bilateral salpingo-oophorectomy
3	Menorrhagia	Dilatation and curettage
4	Menorrhagia	Hysterectomy and bilateral salpingo-oophorectomy
1	Pelvic infection	Hysterectomy and bilateral salpingo-oophorectomy

Procedure

The patient was placed in the supine position with the buttocks slightly elevated. The cervix and posterior fornix were exposed with a Cusco vaginal speculum and between 10 and 15 mCi of 99m Tc-labelled human albumin microspheres (HAM) in a volume of less than 3 ml was

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deposited in the posterior fornix. The patient was kept in this position for about 2 hours. The vulva was covered with a sanitary towel, and the legs were pressed together to prevent the radionuclide solution streaming from the vagina and thus lowering count levels.

In a few cases images were obtained, 4 and 24 hours after deposition of the radioactive tracer, with a Nuclear Chicago Pho/Gamma III scintillation camera (Figs 1 and 2). In most cases a count was performed on removed surgical specimens as a whole or separately on the uterus

and adnexae, for 1 000 seconds in a 12.7-cm well scintillation detector. In one case a piece of the anterior peritoneum, fluid from the pouch of Douglas and blood were also included in the count, to determine the possibility of reabsorption into the bloodstream from the vaginal mucosa.

Radiation exposure to the patients was low owing to the short half-life of ^{99m}Tc (6 hours), and in most cases it was almost negligible since the target organs had been surgically removed.

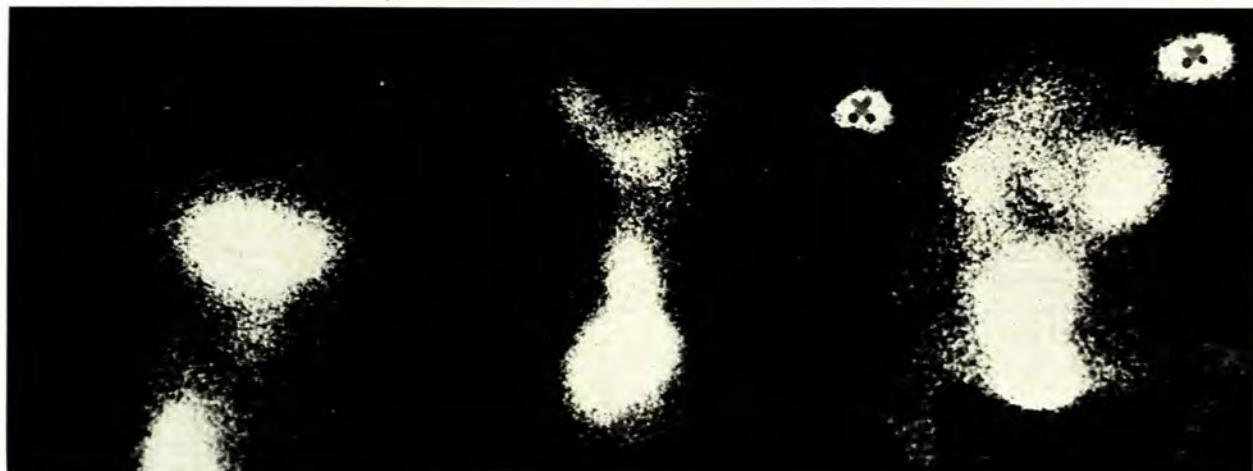


Fig. 1. Scintiphotos showing positive ^{99m}Tc -HAM migration: A — from the vagina to the uterus (4 hours after deposition); B — in both tubes (6 hours after deposition); C — reaching the peritoneal cavity and ovaries 24 hours after deposition (markers in the anterior superior iliac spines).

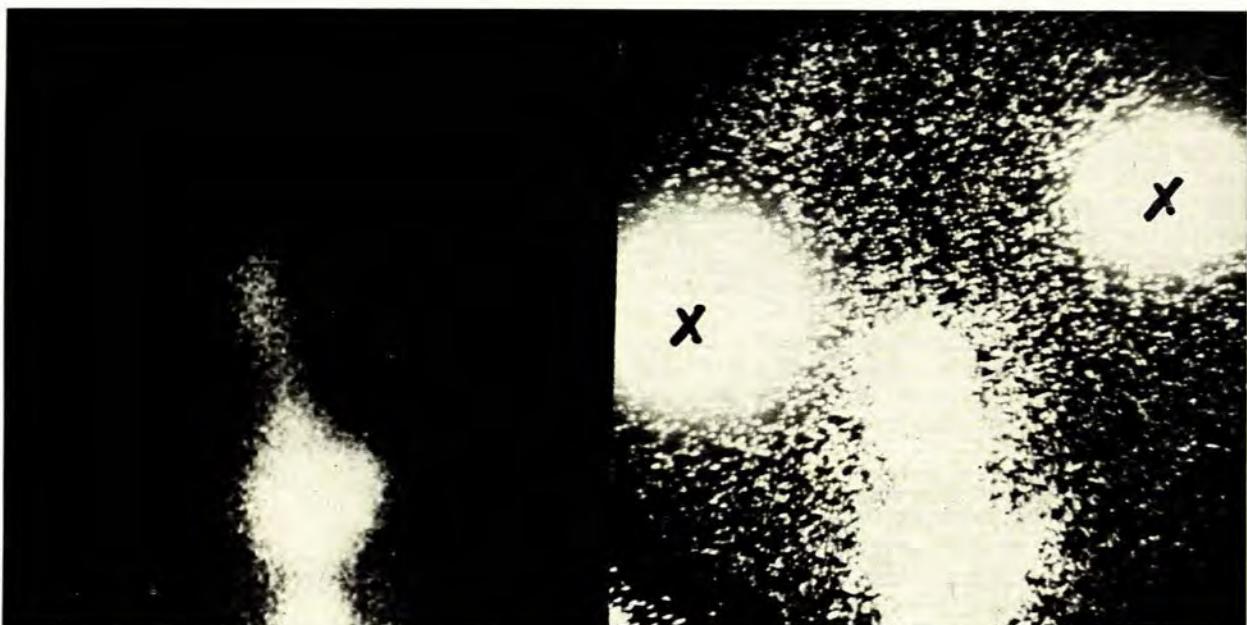


Fig. 2. Scintiphotos showing negative ^{99m}Tc -HAM migration: A — in the left tube (4 hours after deposition); the right tube is patent; B — in both tubes; 24 hours after deposition radioactivity remains in the uterus (markers in the anterior superior iliac spines).

2 June 1979

RESULTS

A total of 24 patients were examined. Because radionuclide material streamed away from the vagina in 3 patients, these cases were considered technically defective and were not included in the final analysis.

Of the remaining 21 cases 16 were positive, that is sufficiently high radioactivity levels were obtained as evidence of migration of the radioactive tracer to the uterus or the tubes and ovaries. The results were negative in 5 cases; in 2 of them the radioactive microspheres did not pass from the vagina to the uterus and in the other 3 there was no migration to the adnexae or fimbria. In the latter, it was impossible to determine radioactivity levels in the uterus because the latter was not removed.

TABLE II. SUMMARY OF RESULTS

Patient	Tissue examined	Radioactivity present (+) or absent (-)
1	Organ imaging fimbria	Uterus, adnexa, fimbria +
2	Organ imaging	Uterus and adnexa +
3	Organ imaging fimbria	Uterus, adnexa, fimbria +
4	Organ imaging adnexa	Uterus +, adnexa +
5	Uterus and adnexa	Uterus +, adnexa -
6	Endometrium	Endometrium -
7	Organ imaging endometrium	Uterus and endometrium +
8	Organ imaging endometrium	Uterus and endometrium -
9	Endometrium	Endometrium +
10	Uterus and adnexa	Uterus and adnexa +
11	Adnexa	Adnexa +
12	Uterus and adnexa	Uterus and adnexa +
13	Uterus and adnexa	Uterus, adnexa +
14	Endometrium	Endometrium +
15	Uterus and adnexa	Uterus +, adnexa -
16	Adnexa	Adnexa +
17	Adnexa	Adnexa +
18	Fimbria	Fimbria -
19	Uterus and adnexa	Uterus and adnexa +
20	Adnexa	Adnexa -
21	Adnexa	Adnexa -

In 14 out of 21 cases it was possible to measure radioactivity levels in the adnexa separately from the uterus. Nine of these showed marked radioactivity in the tubes and ovaries, while in 5 the radioactivity levels were not much higher than the background. In all 5 of these patients, severe tubal occlusion due to previous infection was confirmed by study of the removed specimens (Table II).

In 1 case, radioactivity levels in blood were not much higher than in the background, which indicated that radioactive tracer had not reached the adnexa through the blood supply owing to local reabsorption in the vaginal mucosa.

DISCUSSION

Evidence is available for migration of different substances in either direction within the female reproductive system between the peritoneal cavity and ovaries via the tubes, uterus and vagina, and the outside. Various living organisms actively follow this pathway in both directions. Gases, fluids, dyes and contrast media can easily be introduced from the vagina into the peritoneal cavity. If transit can take place so easily, it is probably the same for many chemical substances used for hygienic, cosmetic or medicinal purposes, many of which may have potential carcinogenic or irritating properties.

To prove this would be of great practical value, because migration of certain chemical substances could play an important aetiological role in gynaecological diseases and especially in carcinoma of the ovary.

We found the use of a particulate radioactive agent such as $^{99m}\text{Tc-HAM}$ with a size range of 30-50 μm to be a suitable and safe means of imaging and evaluating tubal patency and demonstrating the possibility of transit of particles from the vagina to the peritoneal cavity and ovaries.

Results obtained by this technique correlated with findings in the surgically removed specimens, thus demonstrating the accuracy of this radionuclide procedure.

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